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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/296,534	04/22/1999	ROBERT HALLOWITZ	BIOTI-7	8502

33449 7590 10/25/2002

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EXAMINER
ZEMAN, ROBERT A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 10/25/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/296,534	Applicant(s) HALLOWITZ ET AL.	
	Examiner Robert A. Zeman	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-19* is/are pending in the application.

4a) Of the above claim(s) *17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13,15,16,18 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-13 and 15-19* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments and responses filed on 8-26-02 are acknowledged. Claims 2-13, 15-16 and 18-19 have been amended. Claim 17 remains withdrawn from consideration. Claims 1-13, 15-16 and 18-19 are pending and currently under examination.

This application contains claim 17 drawn to an invention non-elected with traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

The objection to the specification with regard to the priority statement is maintained. The amendment to the specification corrected the improper reference to Application 09/139,633. However, due to said amendment the priority statement now reads, "This application is **related to** U.S. Ser. No...". This phrasing is improper. Said statement must reflect how the instant Application is related to the priority document (i.e. a continuation, continuation-in-part etc.).

Oath/Declaration

The objection based on the oath or declaration being defective is maintained for reasons of record. The oath still fails to identify priority documents by application number and filing date herein. Applicant has indicated that they are taking steps to locate the inventors in order to execute a new declaration.

Claim Objections Withdrawn

The objection to claims 2-13 and 15-16 for not being introduced by an article is withdrawn in light of the amendment thereto.

Claim Rejections Withdrawn

The rejection of claims 18 and 19 under 35 U.S.C. 112, second paragraph, as being rendered vague and indefinite by the use of the phrase "under effective conditions" is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 18-19 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained for reasons of record.

Claims 18 and 19 still fail to recite active method steps that read on the preamble of the claims. The amended claims recite the phrase "whereby said latent viral load is the determined number of cells". It is unclear how this is correlated to the viral load **in a host** or even if such a correlation can be made.

Claims 18 and 19 are still rendered vague and indefinite by the use of the term "cell population". It is unclear what cell population Applicant is utilizing since the amended claims

recite, "a cell population comprising intact cells susceptible to HIV-infection expressing cell surface gp120". Is Applicant claiming that said cell population is infected cells?

Claim 19 is still incomplete because the preamble of the amended claim recites "A method of determining latent viral load **in a host**" but there is no language that serves to correlate the result of "determining the number of cells expressing gp120" with "determining viral load". As outlined above, the amended claims recite the phrase "whereby said latent viral load is the determined number of cells". It is unclear how this is correlated to the viral load **in a host** or even if such a correlation can be made.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejections of claims 1-13, 15-16 and 18-19 under 35 U.S.C. 103(a) as being unpatentable over Chun et al. (Nature Vol. 387, pages 183-188, May 1997) in view of Chun et al. (Nature Medicine, Vol. 1, No. 12, pages 1284-1290, December 1995) and Essex et al. (U.S. Patent 4,725,669) and the rejection of claims 13-19 under 35 U.S.C. 103(a) as being unpatentable over Chun et al. (Nature Vol. 387, pages 183-188, May 1997) in view of Chun et al. (Nature Medicine, Vol. 1, No. 12, pages 1284-1290, December 1995) and Essex et al. (U.S. Patent 4,725,669) and Chun et al. (Journal of Experimental Medicine, Vol. 188 No. 1, July 6, 1998 pages 83-91) are maintained for reasons of record.

Applicant argues (Supplemental response 8-26-02):

1. The skilled worker would have been uncertain whether gp120 could be used as a measure of latent viral load.

2. Fessel et al. disclose that circulating viral RNA did not encode high numbers of infectious viral particles.

3. Fessel et al. refers to the paradoxical response to HAART in that their CD4+ PBMC levels increase substantially but their levels of plasma HIV RNA remain high.

4. Based on the type of literature cited in the Office Action, the skilled might have been led to believe that serum concentration of HIV RNA were a reliable indicator of the progression of HIV infection.

5. The literature demonstrates in many cases there was not a correlation between the high levels of serum HIV RNA and the severity of disease and thus, until a particular biochemical marker associated with HIV infection was analyzed one could not have predicted whether a given marker could be used to determine latent viral load. Consequently, there would have been no motivation with an expectation of success to modify the prior art.

Applicant argues (Initial Response 8-26-02)

6. All cited references utilize lysed cells for analysis.

7. There is no motivation to analyze intact cells.

8. Essex does not remedy the deficiencies of Chen because a teaching that a cell surface antigen exists does not make substitution of that antigen for a fundamentally different antigen or a different molecule equivalent or obvious.

9. There is no teaching in the cited prior art that detection of p24 or HIV DNA correlates with or is equivalent to gp120 measure.

10. Fessel et al. supports the argument that one measure of HIV cannot be substituted with another.

Applicant's arguments have been fully considered and deemed non-persuasive.

With regard to Applicant's assertion that one of ordinary skill in the art would be uncertain whether gp120 could be used as a measure of latent viral load in view of the disclosure of Fessel et al: Fessel et al. deals with the correlation of viral RNA with the progression of HIV infection and not the expression of a viral protein. Contrary to Applicant's assertion, it was well known at the time of the invention that gp120 was a marker of HIV infection. This is not only illustrated by the cited reference by Essex et al. but by Virology textbooks. Fields Virology 3rd Edition (Lippincott Williams & Wilkins, Philadelphia, PA 1996) discloses on page 1893, "Gp120, also designated the SU subunit, is a highly glycosylated, hydrophilic protein positioned on the external surface of virion membranes **as well as plasma membranes of infected cells**". Therefore, since gp120 is only expressed on the membranes of infected cells, one of ordinary skill in the art would have had a high expectation of success in using gp120 as the marker in the differential expression method of Chun et al. With regard to Applicants assertion that Fessel et al. supports the argument that one measure of HIV cannot be substituted with another: the disclosure by Fessel et al. deals with RNA expression and the progression of HIV infection and not the expression of a viral protein and hence any conclusions, whether proper or improper, cannot be applied to the expression of viral proteins and its correlation with HIV infection.

Additionally, contrary to Applicant's assertion that a teaching that a cell surface antigen exists does not make substitution of that antigen for a fundamentally different antigen or a different molecule equivalent or obvious, all markers that are unique to the infected state of cell are deemed functional equivalents with regard to determining cell status. Moreover, one of ordinary skill in the art would not only be motivated to use a marker that would streamline his methodology, he or she would have a high expectation of success

Finally, with regard to Applicant's assertion that Chun et al. did not utilize intact cells: Applicants is reminded that both Chun et al. references utilize intact cells (see figure 1 and page 1289 of Chun et al. Nature Medicine Vol. 1 No. 12, pages 1274-1290, which was also cited as the methods used in Chun et al. Nature Vol. 387, pages 183-188, May 1997).

New Grounds of Rejection

35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 18 and 19 are rendered vague and indefinite by the use of the term "capable of". Having the capacity to perform a function is different than actually performing said function. As written, it is impossible to determine the metes and bounds of the claimed invention.

The method steps of claims 18 and 19 are confusing and do not correlate with the intended purpose of said steps as stated in the preamble of the claim. The initial cell population, as recited in the amended claims, is drawn to HIV-susceptible cells expressing gp120. This is the definition of an infected cell. Therefore, it would be impossible to determine a latent viral load based on gp120 expression if all the cells in the cell population express gp120 from the onset of the method.

Claims 18 and 19 are rendered vague and indefinite by the use of the phrase "depleting a cell population comprising...". Depleting the population of what? As written, it is impossible to determine the metes and bounds of the claimed invention.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 608-7991. The examiner can normally be reached on Monday- Thursday 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (703) 308-3909. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

LYNETTE R. F. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Robert A. Zeman
October 24, 2002